

REMARKS/ARGUMENTS

Claims 36-82 are pending. These claims track and find support in the original claim set. Specific support for independent Claim 36 is found in original Claim 1 and on page 4, lines 4 and 13, of the specification which describes SEQ ID NO: 1 and fragments of SEQ ID NO: 1 and on page 4, lines 31-page 5, line 4, which describes sequences which are at least 90-95% identical to SEQ ID NO: 1 and which encode polypeptides with adenosyl homocysteinase activity. Support for independent Claim 69 is found in original Claim 1 and on page 5, lines 8-13, which described polypeptides which are at least 90-95% identical to SEQ ID NO: 2 and which have adenosyl homocysteinase activity. Support for independent Claim 75, directed to sequences which crosshybridize to SEQ ID NO: 1 is found on page 9 of the specification and lines 13-31 describe specific hybridization and washing conditions. Support for Claims 79-81, directed to polynucleotide fragments is found in original Claim 1 and on page 4, lines 21-26, of the specification. Claim 82 finds support in original Claims 20 and 26 and on page 26 of the specification. Accordingly, the Applicants do not believe that any new matter has been added.

New Claims 49-52, 57-60, 65-68, 74 and 78 are process claims, which have been drafted to depend from host cell claims falling within the previously elected Group.

The Applicants thank Examiner Fronda for the courteous and helpful discussion of October 22, 2003. To address the prior art rejections over Pawar et al., it was suggested that the claim set be revised to indicate that the polynucleotide sequences are at least 90-95% identical to SEQ ID NO: 1 or encode polypeptides which are at least 90-95% identical to SEQ ID NO: 2. To help address the enablement and description rejections, the Applicants were advised to describe the claimed polynucleotides using a functional limitation such as "encoding a polypeptide having the adenosyl homocysteinase activity". The deposit rejection could be addressed by perfecting the deposit requirement by making the required statement

regarding continued availability. The Applicants have now made the suggested changes and statement. Accordingly, favorable consideration is now respectfully requested.

#### Election/Restriction

Group I, directed to polynucleotides, vectors and host cells was previously elected. The Applicants note that the Restriction Requirement has been made FINAL. New Claims 49-52, 57-60, 65-68, 74 and 78 are process claims, which have been drafted to depend from host cell claims falling within the previously elected Group. The Applicants respectfully request that these process claims be rejoined upon an indication of allowability for the underlying product (host cell) claims; see MPEP 821.04.

#### Rejection—35 U.S.C. §112, first paragraph

Claims 1-3, 5, 6 and 18 were rejected under 35 U.S.C. 112, first paragraph, on two grounds as lacking adequate description or lacking adequate enablement. This rejection is moot in view of the cancellation of these claims. The Applicants respectfully submit that it would not apply to the new claims which are described in terms of a specific functional activity, i.e., “encodes a polypeptide having the enzymatic activity of adenosyl homocysteinase” and structurally, i.e., by reference to “90-95% identity”, to specific hybridization conditions or to specific SEQ ID NOS.

#### Rejection—35 U.S.C. §112, first paragraph

Claim 9 was rejected under 35 U.S.C. 112, first paragraph, as lacking adequate deposit information for the *E. coli* strain deposited as DSM 14316. New Claim 82 corresponds to Claim 9. *Escherichia coli* strain DH5 $\alpha$ mcr/pEC-XK99sahHalex was deposited as DSM 14316 under the terms of the Budapest Treaty (see page 21, lines 1-3, of

the specification). As required by 37 C.F.R. 1.808, subject to the one exception permitted by 37 C.F.R. 1.808(b), all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon granting of the patent. See MPEP 2410.01.

Rejection—35 U.S.C. §112, second paragraph

Claims 1-3, 5, 6 and 18 were rejected under 35 U.S.C. 112, second paragraph as being indefinite. These rejections are moot in view of the cancellation of these claims.

Rejection—35 U.S.C. §102(b)

Claim 1 was rejected under 35 U.S.C. 102(b) as being anticipated by Pawar et al., Accession AF262755. This rejection is moot in view of the cancellation of Claim 1 and would not apply to the present claims, such as Claim 36, 69 and 75, which now requires a polynucleotide encoding a polypeptide having adenosyl homocysteinase activity. Pawar is directed to a protein encoding S-adenosyl-L-hydrolase. Claims 79-81 are directed to polynucleotide fragments 30 consecutive nucleotides or longer. The longest match in Pawar appears to be between bases 775-802 (Db) which is only 28 polynucleotides.

Rejection—35 U.S.C. §102(b)

Claim 5 was rejected under 35 U.S.C. 102(b) as being anticipated by Pawar et al., Accession AF262755. This rejection is moot in view of the cancellation of Claim 5 and would not apply to the present claims, such as Claim 75, which now requires a polynucleotide encoding a polypeptide having adenosyl homocysteinase activity and which recites specific hybridization conditions.

### Information Disclosure Statement

The information disclosure statement (IDS) filed February 12, 2002 cites documents disclosed in the International Search Report for PCT/EP01/08222. Form 1449 for this IDS considered August 20, 2003 and returned to the Applicants shows the entries for Germany 38 23 451 and Europe 0 435 132 crossed out. English language abstracts for these two documents are provided herewith. Accordingly, the Applicants respectfully request return of a copy of this form showing that these two documents have now been considered.

### Allowable Subject Matter

The Applicants thank Examiner Fronda for indicating that the subject matter of Claims 4 and 7, subject to an objection for dependence on a rejected base claim, is otherwise in condition for allowance.

### CONCLUSION

In view of the above amendments and remarks, the Applicants respectfully submit that this application is now in condition for allowance. Early notification to that effect is earnestly solicited.

Respectfully submitted,

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(OSMMN 08/03)

AN 112:234001 CA  
 ED Entered STN: 23 Jun 1990  
 TI Lysine from recombinant microorganisms  
 IN Cremer, Josef; Eggeling, Lothar; Sahm, Hermann  
 PA Kernforschungsanlage Juelich G.m.b.H., Germany; Degussa A.-G.  
 SO Ger. Offen., 7 pp.  
 CODEN: GWXXBX  
 DT Patent  
 LA German  
 IC ICM C12N001-21  
 ICS C12N015-03; C12P013-08; C12P019-34  
 ICA C07H021-04; C12P019-34; C12P013-08  
 CC 16-2 (Fermentation and Bioindustrial Chemistry)  
 Section cross-reference(s): 3

## FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3823451	A1	19900118	DE 1988-3823451	19880711 <--
	DE 3823451	C2	19970220		
PRAI	DE 1988-3823451		19880711		

AB The gene for aspartate semialdehyde dehydrogenase (asd) or for dihydropicolinate synthase (dapA) or for both enzymes are cloned in plasmid pZ1k, which is used to transform *Corynebacterium glutamicum*. The recombinant bacteria are high producers of L-lysine. Thus, the dapA-contg. plasmid pDA3 of *E. coli* RDA8 and vector pZ1 were both digested with restriction enzymes PstI and SmaI. The vector was treated with phosphatase and the fragments were ligated. The recombinant plasmid pZ1dapt was incubated with protoplasts of *C. glutamicum* to cause its transformation. The transformed bacteria were cultured at 30.degree. for 72 h with stirring in a medium contg. glucose, (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub>, CaCO<sub>3</sub>, and mineral salts. The lysine concn. in the medium was 41 mM, compared with 33 mM after fermn. with the parent strain.

ST *Corynebacterium* genetic engineering lysine fermn

IT *Corynebacterium glutamicum*

(lysine manuf. with recombinant)

IT Fermentation

(lysine, with recombinant *Corynebacterium glutamicum*)

IT Genetic engineering

(of *Corynebacterium glutamicum*, for lysine prodn.)

IT Gene and Genetic element, microbial

RL: BIOL (Biological study)

(asd, of *Escherichia coli*, cloning and expression of, in lysine-producing *Corynebacterium glutamicum*)

IT Gene and Genetic element, microbial

RL: BIOL (Biological study)

(dapA, of *Escherichia coli*, cloning and expression of, in lysine-producing *Corynebacterium glutamicum*)

IT 56-87-1P, L-Lysine, preparation

RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)

(manuf. of, with recombinant *Corynebacterium glutamicum*)

AN 1990-023325 [04] WPIX

DNC C1990-010285

TI Recombinant DNA for increasing lysine prodn. - by *Corynebacterium* or *Brevibacterium*, contg. aspartate semi-aldehyde dehydrogenase and/or dihydro di picolinate synthase gene.

DC B05 D16 E16

IN CREMER, J; EGGELING, L; SAHM, H

PA (KERJ) KERNFORSCHUNGSANLAGE JUELICH; (DEGS) DEGUSSA AG; (KERJ) FORSCHUNGSZENTRUM JUELICH GMBH

CYC 1  
 PI DE 3823451 A 19900118 (199004)\* 7p <--  
 DE 3823451 C2 19970220 (199712) 8p C12N015-03 <--  
 ADT DE 3823451 A DE 1988-3823451 19880711; DE 3823451 C2 DE 1988-3823451 19880711  
 PRAI DE 1988-3823451 19880711  
 IC C12N001-21; C12N015-03; C12P013-08; C12P019-34  
 ICM C12N015-03  
 ICS C12N001-21; C12P013-08; C12P019-34  
 AB DE 3823451 A UPAB: 19930928  
 New recombinant DNA mols. (I) capable of replication in Corynebacterium or Brevibacterium cells comprise vector DNA (II) and a DNA fragment (III) contg. a gene coding for aspartate semialdehyde dehydrogenase (asd) and/or dihydrodipicolinate synthase (dapA), where (III) is derived from an Escherichia, Serratia or Klebsiella microorganism.  
 Also claimed are Corynebacterium and Brevibacterium strains contg. (I) and a chromosomal gene coding for L-lysine.  
 USE/ADVANTAGE - The new strains are useful for fermentative prodn. of L-lysine, giving higher yields than the parent strains from which they are derived.  
 0/3  
 FS CPI  
 FA AB; DCM  
 MC CPI: B04-B02B1; B04-B04A1; B10-B01B; D05-C01; D05-H04; D05-H12; E10-B01A3

AN 115:90668 CA  
 ED Entered STN: 06 Sep 1991  
 TI Lysine manufacture with recombinant Corynebacterium or Brevibacterium  
 IN Cremer, Josef; Eggeling, Lothar; Sahm, Hermann  
 PA Forschungszentrum Juelich G.m.b.H., Germany  
 SO Eur. Pat. Appl., 12 pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA German  
 IC ICM C12N015-09  
 ICS C12P013-08; C07H021-04; C12N001-21  
 ICI C12P013-08, C12R001-15; C12P013-08, C12R001-13  
 CC 16-2 (Fermentation and Bioindustrial Chemistry)  
 Section cross-reference(s): 3, 10

## FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 435132	A1	19910703	EP 1990-124557	19901218 <--
	EP 435132	B1	19940817		
	R: BE, DE, FR, GB, IT, NL, SE				
	DE 3943117	A1	19910704	DE 1989-3943117	19891227
PRAI	DE 1989-3943117		19891227		
AB	Lysine manuf. with Corynebacterium or Brevibacterium is made more efficient by introduction of genes for a feedback-insensitive aspartate kinase (I) and for dihydrodipicolinate synthase. The feedback-insensitive I gene is from a Corynebacterium glutamicum. Expression plasmids based upon the expression vector pJCl carrying either or both of these genes were prepd. by std. methods and introduced into a C. glutamicum with a feedback-responsive I. Transformants showed a >10-fold increase in the activities. Yields (72 h, 30.degree., glucose/salts medium) of lysine from transformants were from 0 to 50 mM for C. glutamicum 13032 when both genes were introduced (effects were smaller when only one of the genes was introduced). For C. glutamicum DG52-5 the increase was from 43 to 71 mM.				

ST lysine manuf recombinant Corynebacterium Brevibacterium; aspartate kinase lysine manuf Corynebacterium; dihydropicolinate synthase lysine manuf Corynebacterium

IT Brevibacterium  
Corynebacterium  
Corynebacterium glutamicum  
(lysine manuf. with recombinant, overexpression of lysine biosynthesis genes in relation to)

IT Fermentation  
(lysine, with recombinant Corynebacterium glutamicum)

IT Amino acids, preparation  
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)  
(manuf. of, with recombinant Brevibacterium or Corynebacterium)

IT Molecular cloning  
(of gene for feedback-resistant aspartate synthase of Corynebacterium glutamicum in Escherichia coli)

IT Plasmid and Episome  
(pJC23, dehydropicolinate synthetase gene on, expression in C. glutamicum of, for increased yields in lysine manuf.)

IT Plasmid and Episome  
(pJC30, feedback-resistant aspartate kinase gene of Corynebacterium glutamicum on, expression in C. glutamicum of, for increased yields in lysine manuf.)

IT Plasmid and Episome  
(pJC50, feedback-resistant aspartate kinase gene of Corynebacterium glutamicum and dihydropicolinate synthase genes on, expression in C. glutamicum of, for increased yields in lysine manuf.)

IT Gene and Genetic element, microbial  
RL: BIOL (Biological study)  
(lysC, overexpression in Brevibacterium or Corynebacterium of, for increased yields in lysine manuf.)

IT Gene and Genetic element, microbial  
RL: BIOL (Biological study)  
(dapA, overexpression in Brevibacterium or Corynebacterium of, for increased yields in lysine manuf.)

IT 9012-50-4, Aspartate kinase  
RL: BIOL (Biological study)  
(feedback-resistant, gene for, overexpression in Corynebacterium glutamicum of, for increased yields in lysine manuf.)

IT 9055-59-8  
RL: BIOL (Biological study)  
(gene for, overexpression in Corynebacterium glutamicum of, for increased yields in lysine manuf.)

IT 56-87-1, Lysine, biological studies  
RL: BIOL (Biological study)  
(manuf. with recombinant Brevibacterium or Corynebacterium overexpressing lysine biosynthesis genes)

AN 1991-194725 [27] WPIX

DNC C1991-084237

TI Increasing aminoacid esp. lysine prodn. in Corynebacterium - or Brevibacterium, contg. recombinant DNA with sequences for both dihydro-di picolinate synthase and de-regulated aspartate kinase.

DC B05 D16 E16

IN CREMER, J; EGDELING, L; SAHM, H

PA (KERJ) FORSCHUNGSZENTRUM JUELICH GMBH; (KERJ) FORSCHUNGSZENTRUM JUELICH GMBH

CYC 7

PI EP 435132 A 19910703 (199127)\*  
R: BE DE FR GB IT NL SE  
DE 3943117 A 19910704 (199128)

&lt;--

EP 435132 B1 19940817 (199432) DE 11p C12N015-09 <--  
 R: BE DE FR GB IT NL SE  
 DE 59006837 G 19940922 (199437) C12N015-09  
 ADT EP 435132 A EP 1990-124557 19901218; DE 3943117 A DE 1989-3943117  
 19891227; EP 435132 B1 EP 1990-124557 19901218; DE 59006837 G DE  
 1990-506837 19901218, EP 1990-124557 19901218  
 FDT DE 59006837 G Based on EP 435132  
 PRAI DE 1989-3943117 19891227  
 REP DE 3823451; EP 143195; EP 197335; EP 219027; EP 387527  
 IC C07C229-26; C07H021-04; C12N001-21; C12N015-09; C12P013-08; C12R001-15  
 ICM C12N015-09  
 ICS C07C229-26; C07H021-04; C12N001-21; C12P013-08; C12R001-15  
 ICI C12P013-08, C12R001:15; C12P013-08, C12R001:  
 AB EP 435132 A UPAB: 19930928  
 Prodn. of amino acid, esp. L-lysine (I), comprises growing a  
 microorganism of the genera Corynebacterium or Brevibacterium which  
 contains recombinant DNA consisting of vector DNA and a sequence for  
 prodn. of proteins with dapA (dihydrodipicolinate synthase) activity,  
 in a nutrient medium, and then recovery of amino acid. The new feature  
 is that the DNA additionally contains a sequence encoding protein with  
 lysC (deregulated aspartate kinase) activity.  
 Also new are (1) recombinant DNA contg. dapA and lysC sequence  
 plus vector DNA and (2) (I)-producing Corynebacterium and  
 Brevibacterium contg. such DNA.  
 The DNA coding sequences are esp. derived from a (I)-producing  
 strain, partic. a mutant derived from C. glutamicum ATCC 13032 with  
 reduced feed-back inhibition of aspartate kinase.  
 USE/ADVANTAGE - Transformants contg. the new recombinant DNA have  
 improved amino acid, esp. (I), secretion rates. They have 15-fold  
 higher dapA and aspartate kinase activities (the rate-controlling  
 factors in (I) biosynthesis).  
 0/3  
 FS CPI  
 FA AB; DCN  
 MC CPI: B04-B02B1; B04-B04A1; B10-B01B; B11-A; D05-C01; D05-H03B;  
 D05-H04; D05-H12; E10-B01C; E10-B02D